5,087,571 (hereafter "Leder") and also in view of Todaro *et al.*, (1963) J.Cell. Biol. 17:299-313 (hereafter "Todaro"). In particular, the Examiner is of the opinion that the claimed invention is *prima facie* obvious, reasoning that it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a cell line from the cells of the transgenic mice of Durbin because Leder and Jallat allegedly motivate the artisan to do that and allegedly disclose how to make cell lines from transgenic mice. The Examiner is also of the opinion that the immortalization of these cell lines would be obvious because the immortalization of cells and the desirabilities of immortalization using such tools as SV40 is known in the art.

The present invention is directed to immortalized STAT1- deficient mammalian cell lines.

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed Cir. 1987). Further, Applicants respectfully submit that the Examiner, relying on hindsight, has applied an improper "obvious to try" standard. "[W]hether a particular combination might be 'obvious to try' is not a legitimate test of patentability." In re David H. Fine, 837 F.2d 1071,1074 (Fed. Cir. 1988); 5 U.S.P.Q.2D (BNA) 1596 (citing In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed Cir. 1987); In re Goodwin, 576 F.2d 375, 377, 198 USPQ 1, 3 (C.C.P.A. 1978)). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention." In re David H. Fine, *supra* at 1075.

Durbin teaches making transgenic mice deficient in the *Stat1* gene. As the Examiner acknowledges, Durbin does not teach developing an immortalized cell line from the mouse (Office Action at Page 2, fourth paragraph). In fact, the major focus of Durbin is the creation of *Stat1* $^{-/-}$ mice in order to study the biological function of STAT1 *in vivo*. Specifically, Durbin discusses the creation of a *Stat1* $^{-/-}$ mouse in order to investigate STAT1 involvement in cytokine signaling and "to probe the roles of STAT1- linked pathways under physiologic settings and during development" (Durbin at Page 443). Given the emphasis on discerning the role of STAT1 *in vivo,* Applicants respectfully submit that Durbin actually teaches away from the creation of an immortalized *Stat1*$^{-/-}$ cell line. Thus, Durbin clearly does not disclose, teach or suggest the immortalized STAT1- deficient cell lines of the subject invention and utility of such immortalized cells as hosts for producing viral stocks, for producing recombinant viral vectors, for detecting viruses and the like.

Leder discloses creation of a transgenic mouse containing an activated oncogene and a method for providing a cell culture from the transgenic animal. As this reference does not mention the *Stat1* gene, it does not contemplate, teach or suggest the cell lines of the present invention. Leder, like the other cited references, fails to provide motivation directing one to the present invention.

Likewise, while Jallat may teach methods of creating a cell line from a transgenic mouse, this reference does not disclose, teach or suggest creation of an immortalized *Stat1*$^{-/-}$ cell line or the uses thereof. Jallat discloses a method to create a transgenic liver tumor cell line containing an exogenous DNA sequence for human factor IX and a second exogenous DNA sequence encoding either the SV40 virus T-antigen or the mouse c-myc gene. (Jallat at Column

3, Lines 22-27 and Lines 40-42; Column 4, Lines 15-19). As such, it does not disclose, teach or suggest the present invention.

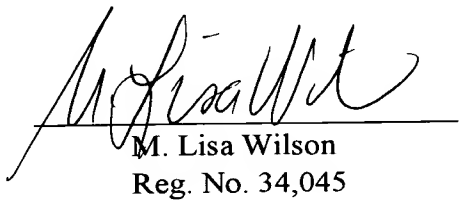
Finally, Todaro discloses that spontaneously immortalized cell lines may be derived from normal Swiss mouse embryo cells (and possibly other cell types) after successive cell culture transfer. The Todaro reference does not mention the *Stat1* gene nor does it discuss creating the immortalized *Stat1*$^{-/-}$ cell lines of the invention. Since the characteristics of the cell lines of the present invention were never contemplated, taught or suggested, the Todaro reference fails to provide motivation directing one to the present invention.

Applicants respectfully submit that the combined teachings of the cited references fail to motivate one of skill in the art to make the present invention particularly where the primary reference (Durbin) fails to provide any motivation to make the claimed invention. Applicants also respectfully submit that one cannot apply an "obvious to try" standard to the combined teachings of Durbin, Jallat, Leder and Todaro to create the STAT1- deficient cells lines of the present invention and to do so is nothing more than employing improper hindsight. Since none of the cited references contemplate, teach or suggest the claimed *Stat1* $^{-/-}$cell lines or their uses, the invention is not *prima facie* obvious and the Applicants respectfully request that the rejection of Claims 1-5 and 35-37 under 35 U.S.C. §103(a) be withdrawn.

In view of the foregoing remarks it is firmly believed that the subject invention is in

condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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